



MARKED-UP VERSION

1. An isolated nucleic acid molecule encoding a fusion polypeptide capable of binding a cytokine to form a nonfunctional complex, comprising:
 - 5 a) a nucleotide sequence encoding a first fusion polypeptide component comprising the amino acid sequence of the cytokine binding portion of ~~the~~ extracellular domain of the specificity determining component of ~~the~~ cytokine's receptor;
 - b) a nucleotide sequence encoding a second fusion polypeptide component comprising the amino acid sequence of the cytokine binding portion of the extracellular domain of the signal transducing component of ~~the~~ cytokine's receptor; and
 - 10 c) a nucleotide sequence encoding a third fusion polypeptide component comprising the amino acid sequence of a multimerizing component.
2. The nucleic acid molecule of claim 1, wherein the nucleotide sequence encoding the first component is upstream of the nucleotide sequence encoding the second component.
- 20 3. The nucleic acid molecule of claim 1, wherein the nucleotide sequence encoding the first component is downstream of the nucleotide sequence encoding the second component.
- 25 4. The isolated nucleic acid molecule of claim 1, wherein the cytokine receptor is the receptor for a member of the hematopoietin family of cytokines selected from the group consisting of interleukin-2, interleukin-3, interleukin-4, interleukin-5, interleukin-6, interleukin-7, interleukin-9, interleukin-11, interleukin-13, interleukin-15, granulocyte macrophage colony stimulating factor, oncostatin M, and leukemia inhibitory factor and
- 30 cardiotrophin-1
5. The isolated nucleic acid molecule of claim 1, wherein the cytokine receptor is the receptor for a member of the interferon family of cytokines selected from the group consisting of IFN-gamma, IFN-alpha, and IFN-beta.
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6. The isolated nucleic acid molecule of claim 1, wherein the cytokine receptor is the receptor for a member of the immunoglobulin superfamily of cytokines selected from the group consisting of B7.1 (CD80) and B7.2 (B70).
- 5 7. The isolated nucleic acid molecule of claim 1, wherein the cytokine receptor is the receptor for a member of the TNF family of cytokines selected from the group consisting of TNF-alpha, TNF-beta, LT-beta, CD40 ligand, Fas ligand, CD 27 ligand, CD 30 ligand, and 4-1BBL.
- 10 8. The isolated nucleic acid molecule of claim 1, wherein the cytokine receptor is the receptor for a member of the TGF- β /BMP family selected from the group consisting of TGF- β 1, TGF- β 2, TGF- β 3, BMP-2, BMP-3a, BMP-3b, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8a, BMP-8b, BMP-9, BMP-10, BMP-11, BMP-15, BMP-16, endometrial bleeding associated factor (EBAF), growth differentiation factor-1 (GDF-1), GDF-2, GDF-3, GDF-5, GDF-6, GDF-7, GDF-8, GDF-9, GDF-12, GDF-14, mullerian inhibiting substance (MIS), activin-1, activin-2, activin-3, activin-4, and activin-5.
- 15 9. The isolated nucleic acid molecule of claim 1, wherein the cytokine receptor is the receptor for a cytokine selected from the group consisting of interleukin-1, interleukin-10, interleukin-12, interleukin-14, interleukin-18 and MIF.
- 20 10. The isolated nucleic acid molecule of claim 1, wherein the multimerizing component comprises an immunoglobulin derived domain.
- 25 11. The isolated nucleic acid molecule of claim 10, wherein the immunoglobulin derived domain is selected from the group consisting of the Fc domain of IgG, the heavy chain of IgG, and the light chain of IgG.
- 30 12. A fusion polypeptide encoded by the isolated nucleic acid molecule of claim 1.

13. A composition capable of binding a cytokine to form a nonfunctional complex comprising a multimer of the fusion polypeptide of claim 12.
14. The composition of claim 13, wherein the multimer is a dimer.
- 5 15. A vector which comprises the nucleic acid molecule of claim 1.
16. An expression vector comprising a nucleic acid molecule of claim 1, wherein the nucleic acid molecule is operatively linked to an expression
10 control sequence.
17. A host-vector system for the production of a fusion polypeptide which comprises the expression vector of claim 16, in a suitable host cell.
- 15 18. The host-vector system of claim 17, wherein the suitable host cell is a bacterial cell, yeast cell, insect cell, or mammalian cell.
19. The host-vector system of claim 17, wherein the suitable host cell is E. coli.
- 20 20. The host-vector system of claim 17, wherein the suitable host cell is a COS cell.
21. The host-vector system of claim 17, wherein the suitable host cell is a
25 CHO cell.
22. The host-vector system of claim 17, wherein the suitable host cell is a 293 cell.
- 30 23. The host-vector system of claim 17, wherein the suitable host cell is a BHK cell.
24. The host-vector system of claim 17, wherein the suitable host cell is a NS0 cell.

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25. A method of producing a fusion polypeptide which comprises growing cells of the host-vector system of claim 17, under conditions permitting production of the fusion polypeptide and recovering the fusion polypeptide so produced.

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The method of claim 25, wherein the host-vector system is a prokaryotic system, and the fusion polypeptide is a fusion of a polypeptide of interest with a polypeptide of a prokaryotic origin, and the fusion polypeptide is recovered from the host-vector system by a method comprising: (a) growing the host-vector system under conditions permitting production of the fusion polypeptide; (b) harvesting the host-vector system; (c) lysing the host-vector system; and (d) separating the fusion polypeptide from the host-vector system.

The method of claim 25, wherein the host-vector system is a eukaryotic system, and the fusion polypeptide is a fusion of a polypeptide of interest with a polypeptide of a eukaryotic origin, and the fusion polypeptide is recovered from the host-vector system by a method comprising: (a) growing the host-vector system under conditions permitting production of the fusion polypeptide; (b) harvesting the host-vector system; (c) lysing the host-vector system; and (d) separating the fusion polypeptide from the host-vector system.

The method of claim 25, wherein the host-vector system is a prokaryotic system, and the fusion polypeptide is a fusion of a polypeptide of interest with a polypeptide of a prokaryotic origin, and the fusion polypeptide is recovered from the host-vector system by a method comprising: (a) growing the host-vector system under conditions permitting production of the fusion polypeptide; (b) harvesting the host-vector system; (c) lysing the host-vector system; and (d) separating the fusion polypeptide from the host-vector system.

The method of claim 25, wherein the host-vector system is a eukaryotic system, and the fusion polypeptide is a fusion of a polypeptide of interest with a polypeptide of a eukaryotic origin, and the fusion polypeptide is recovered from the host-vector system by a method comprising: (a) growing the host-vector system under conditions permitting production of the fusion polypeptide; (b) harvesting the host-vector system; (c) lysing the host-vector system; and (d) separating the fusion polypeptide from the host-vector system.

The method of claim 25, wherein the host-vector system is a prokaryotic system, and the fusion polypeptide is a fusion of a polypeptide of interest with a polypeptide of a prokaryotic origin, and the fusion polypeptide is recovered from the host-vector system by a method comprising: (a) growing the host-vector system under conditions permitting production of the fusion polypeptide; (b) harvesting the host-vector system; (c) lysing the host-vector system; and (d) separating the fusion polypeptide from the host-vector system.